REMARKS

I. Status of the Claims

Claims 1-101 were filed with the application. Claims 1-58, 60, 63-69 and 71-101 have been canceled. Thus, claims 59, 61, 62 and 70 are under consideration and have been examined. Claims 59, 61, 62 and 70 are again presented for reconsideration. The claims are rejected under 35 U.S.C. §112, second paragraph, 35 U.S.C. §102 and 35 U.S.C. §103. Claims 59, 62 and 70 stand rejected under 35 U.S.C. §102. The specific grounds for rejection, and applicants' response thereto, are set out in detail below.

II. Rejections Under 35 U.S.C. §112, Second Paragraph

The examiner has rejected claims 59, 61, 62 and 70 under the second paragraph of §112 as being indefinite for failing to particularly point out and distinctly claim the subject matter.

Claim 59 is rejected for use of the term "small molecule modulator." Applicants traverse. The term "small molecule" brings up 1.18 ***million*** hits on a Google® search. It is impossible to argue that this term is not understood by those in the field given such overwhelming evidence to the contrary. Therefore, the rejection is improper.

Claim 70 is also rejected over the term "second pharmaceutical agent." Applicants previously amended claim 70 to clarify that the second pharmaceutical agent is distinct from the agent provided in claim 59. Applicants have previously attempted to amend claim 59 to specify a first pharmaceutical agent (*i.e.*, the modulator), in that claim, but entry of this amendment was denied. Applicants are more than willing to provide an additional amendment, or authorize the examiner to make such an amendment. Even if this amendment is not entered, however, applicants submit that one of skill in the art would recognize that the "second pharmaceutical

agent" of claim 70 is in addition to the modulator of claim 59, and thus there is no issue of indefiniteness. Again, this rejection is improper and should be withdrawn.

III. Rejections Under 35 U.S.C. §102(e)

A. Sussman *et al.*

Claims 59, 62 and 70 stand rejected under 35 U.S.C. §102(b) for allegedly being anticipated by Sussman *et al.* According to the examiner, the use of calcineurin in transgenic mice anticipates the claims. Applicants traverse.

Reference to claim 59, the only independent claim under consideration, with reveal that the subject to be treated must be a ***human***. A mouse, transgenic or not, is not a human. Therefore, the rejection is improper and should be withdrawn.

B. U.S. Patent 4,330,557

Claims 59, 61 and 70 are rejected under 35 U.S.C. §102(b) over U.S. Patent 4,330,557. Applicants traverse.

The examiner argues that because certain fatty acids activate calcineurin, and calcineurin activates MCIP, the '557 patent anticipates applicants' claims. What is missing from this analysis, however, is the ***knowledge*** that calcineurin regulates MCIP, which can only be found in applicants' specification. In order to make the deficiency in the '557 patent more clear, applicants have amended the claims to more precisely state that the small molecule is selected on the basis of it's MCIP modulating function. The cited reference clearly fails to provide information necessary to accomplish this step (inherent functions of calcineurin notwithstanding), and therefore the rejection is improper.

Moreover, the reference fails to teach or suggest the step of "identifying a human subject in need of striated muscle cell growth modulation" as the '557 patent deals with patients suffering from shock or trauma. Thus, for a second reason, the rejection is improper.

C. U.S. Patent 5,651,980

Claims 59 and 62 are rejected under 35 U.S.C. §102(b) over U.S. Patent 5,651,980. Applicants traverse.

The examiner argues that because cyclosporing inhibits calcineurin, and calcineurin activates MCIP, the '980 patent anticipates applicants' claims. What is missing from this analysis, however, is the ***knowledge*** that calcineurin regulates MCIP, which can only be found in applicants' specification. In order to make the deficiency in the '980 patent more clear, applicants have amended the claims to more precisely state that the small molecule is selected on the basis of it's MCIP modulating function. The cited reference clearly fails to provide information necessary to accomplish this step (inherent functions of calcineurin notwithstanding), and therefore the rejection is improper.

Moreover, the reference fails to teach or suggest the step of "identifying a human subject in need of striated muscle cell growth modulation" as the '980 patent deals with patients suffering from inflammatory responses in transplant scenarios. Thus, for a second reason, the rejection is improper.

D. U.S. Patent 5,958,404

Claims 59, 62 and 70 are rejected under 35 U.S.C. §102(b) over U.S. Patent 5,958,404.

The examiner argues that because cyclosporin inhibits calcineurin, and calcineurin activates MCIP, the '404 patent anticipates applicants' claims. What is missing from this analysis, however, is the ***knowledge*** that calcineurin regulates MCIP, which can only be found in applicants' specification. In order to make the deficiency in the '404 patent more clear, applicants have amended the claims to more precisely state that the small molecule is selected on the basis of it's MCIP modulating function. The cited reference clearly fails to provide information necessary to accomplish this step (inherent functions of calcineurin notwithstanding), and therefore the rejection is improper.

Moreover, the reference fails to teach or suggest the step of "identifying a human subject in need of striated muscle cell growth modulation" as the '404 patent deals with patients suffering from inflammatory responses in transplant scenarios. Thus, for a second reason, the rejection is improper.

IV. Rejections Under 35 U.S.C. §103

Claims 59, 61, and 62 are rejected under 35 U.S.C. §103(a) as allegedly being obvious in light of Chin *et al.*, and Sussman *et al.* The examiner alleges that these references, which teach the inhibition of calcineurin with calcineurin inhibitors, render obvious the claims of modulating MCIP, since MCIP was later found to be both activated by and capable of modulating the activity of calcineurin. Applicants traverse.

Applicants again contend, as stated many times in prior responses and briefs, that in order to make modulation of MCIP obvious in light of these references, the examiner is improperly relying on inherency in the context of an obviousness rejection, ***since MCIP's relation to calcineurin was not known at the time these references published.*** A proper analysis of

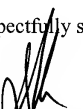
references used to support an obviousness rejection should focus on whether the references would render the invention obvious based on the knowledge that one of skill in the art would gain from the references, not based on what is later discovered to be true. The fact that a specific result or pathway might flow inherently from the practice of a process or discovery of a partial biological pathway is immaterial if the skilled artisan "would not appreciate or recognize that inherent result." *In re Naylor*, 152 USPQ 106 (CCPA 1966). Furthermore, *In re Spormann*, 150 USPQ 449 (CCPA 1966) says that "the inherency of an advantage and its obviousness are entirely different questions. That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown." That statement describes the current situation precisely since both of the cited references existed before the knowledge of MCIP's role in cardiac biology was fully elucidated. The fact that it was later discovered that calcineurin could modulate MCIP would not and could not make it obvious to one of skill in the art, prior to that discovery, that modulating MCIP could be accomplished by modulating calcineurin. In other words, since MCIP's relationship to calcineurin was "unknown" at the time these references published, they cannot be used as "predicates" for an obviousness rejection.

Perhaps more to the point, applicants submit neither reference renders obvious the combined steps of (i) selecting a human patient in need of a muscle growth modulating therapy, (ii) selecting a small molecule for its ability to modulate MCIP, and (iii) treating the selected human patient. Thus, the examiner has simply ignored required elements of the claims, relying instead on the flawed inherency argument to support an obviousness rejection. As stated above, this is not proper. In light of these statements, reconsideration and reversal of these rejections is respectfully requested.

IV. Conclusion

In light of the foregoing, applicants respectfully submit that all claims are in condition for allowance, and an early notification to this effect is earnestly solicited. Should the examiner have any questions regarding this response, he is invited to contact the undersigned attorney at (512) 536-3184 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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